

REMARKS

Claims 45-50 are pending in this application. Claims 45, 47 and 49 have been amended to more clearly indicate that at least one of the nucleosides of the claimed compounds is a 5'-O- terminal nucleoside having, respectively, a non-aromatic lipophilic molecule, a non-aromatic molecule, or a lipophilic molecule linked to the 5'-O-position of the nucleoside. A proviso has also been added to provide that the compounds do not include sulfamate or sulfamide internucleotide linkages. No new matter is entered by these amendments.

As a preliminary matter, Applicants wish to thank Examiner Jezia Riley for the personal interview with their representative, Herb Boswell, on October 6, 2005. During the interview, Mr. Boswell proposed limiting the claims to the 5'-O- terminal positions as delineated in the amendments provided herewith. In distinguishing the cited art (U.S. Pat. No. 5,470,967, the "Huie patent", and U.S. Pat. No. 5,015,733, the "Smith patent") from the claimed invention, Mr. Boswell pointed out that the Huie patent is directed to the inclusion of sulfamate internucleotide linkages in oligonucleotides in order to achieve desired properties and in fact, the claims of the Huie patent all specify the presence of at least one sulfamate internucleotide linkage within the claimed oligonucleotides. Accordingly, Mr. Boswell explained how one of ordinary skill in the art would not look to the Huie patent for guidance in providing the presently claimed compounds. The Examiner and Mr. Boswell discussed adding a proviso to exclude the sulfamate and sulfamide internucleotide linkages described in the Huie patent. Mr. Boswell further noted that in the Smith patent the conjugate molecules are linked to the nucleotides via a nitrogen atom directly connected to a carbon atom, be it C-2', C-3' or C-5', of the sugar portion of the nucleotide. The proposed amended claims discussed with the examiner and submitted herein, exclude such direct nitrogen-C-5' linkages since they required the presence of a 5'-O-, *i.e.*, an oxygen-C-5' linkage.

II. Double Patenting Rejections

Claims 45-50 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 21 of U.S. Patent No. 6,153,737 to

Manoharan *et al.* Although Applicants do not necessarily agree, they are filing a terminal disclaimer herewith to advance prosecution.

III. Rejections Under 35 U.S.C. § 103

Claims 45-50 stand rejected under 35 U.S.C. § 103 as allegedly being unpatentable over the Huie patent in view of the Smith patent. Applicants respectfully traverse this rejection because one of ordinary skill in the art would not be motivated to combine the Huie and Smith patents in the manner suggested in the Office action to produce compounds having a non-aromatic lipophilic molecule, a non-aromatic molecule, or a lipophilic molecule linked to the 5'-O-position of a nucleoside (*i.e.*, via an **oxygen** atom) that do not include sulfamate or sulfamide internucleotide linkages. Instead, the Smith patent is directed to covalently attaching fluorescent dyes or other detectable moieties through **amino** groups (*e.g.*, via a **nitrogen** atom) that are directly connected to a carbon atom, be it C-2', C-3' or C-5' of the sugar portion of a nucleotide within the oligonucleotide. Thus in all instances in the Smith patent, the detectable molecule would be linked to the oligonucleotide via a 2'-deoxy-2'-amino or 3'-deoxy-3'-amino or 5'-deoxy-5'-amino linkage.

The Huie patent is directed to preparing oligonucleotides possessing at least one **sulfamate** or **sulfamide** internucleotide linkage. Huie states at column 5, lines 51 to 56 "Applicants have generated a list of chemical, biochemical, and structural criteria which, if met by a compound, are likely to lead to superior functions such as anti-sense, anti-viral and triplex functions. The linkage should be:..." This is followed by a list of seven criteria. Huie further states at column 5, lines 61 to 63: "Applicants have developed compounds with at least one novel sulfur-centered linkages which meet all of these criteria. These linkages are sulfamate esters." In the office action the examiner subscribes to Huie compounds having 2'-substituents. Applicants respectfully question, however, what would lead the art skilled to select only 2'-substituents of Huie and ignore the "very essence" of the teachings of Huie, the inclusion of sulfamate ester linkages? There is no such suggestion in Huie – in fact the opposite is true. Huie suggests to the art skilled to incorporate sulfamate ester linkages as part and parcel of compounds likely to exhibit all of the criteria suggested by Huie as important. Huie teaches away from Applicants' invention.

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Since Applicants' claimed compounds having a non-aromatic lipophilic molecule, a non-aromatic molecule, or a lipophilic molecule linked via an oxygen atom at the 5'-O-position of a nucleoside are quite different from the compounds taught in the Huie and Smith patents, Applicants request that the rejection for alleged obviousness be withdrawn.

III. Conclusions

Applicants request the Examiner to:

- (1) enter the amendments to claims 45, 47 and 49;
- (2) reconsider and withdraw the rejections of the claims; and
- (3) pass claims 45-50 to allowance.

If the Examiner wishes to discuss this matter further, she is requested to contact the undersigned attorney at 215-568-3100.

Respectfully submitted,



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